Exclusion and inclusion criteria of the EXPAND trial according to the study protocol

Inclusion criteria:

For inclusion in the study, all of the following inclusion criteria must be fulfilled:

• Written informed consent before any study-related activities are carried out

• Age ≥ 18 years

• Histologically confirmed adenocarcinoma of the stomach or gastroesophageal junction (AEG types I-III according to Siewert classification, see appendix A)

Diagnosis should be based on recently obtained tumor material. The histological sample on which the diagnosis is based must have been obtained no more than 2 years before enrolment into this study.

• Archived tumor material sample for at least subsequent standardized EGFR expression assessment

Investigators must make sure in advance that appropriate archived tumor material is available from a potentially eligible subject, and that a sample can be shipped to a central repository if the subject agrees to participate.

• Unresectable advanced (M0) or unresectable metastatic (M1) disease

In the event of unresectable advanced disease, at least one measurable locoregional lymph node or other measurable extraluminal tumor lesion ≥ 2cm must be documented (irrespective of whether it is measured by conventional techniques or spiral CT scan).

• At least one radiographically documented measurable lesion in a previously nonirradiated area according to RECIST, i.e. this lesion must be adequately measurable in at least one dimension (longest diameter to be recorded) as ≥ 2cm by conventional techniques or ≥ 1 cm by spiral CT scan (see section 7.2). Primary tumor site will be considered as a non-measurable lesion only.

• ECOG performance status 0-1

• Estimated life expectancy > 12 weeks

• Medically accepted contraception (if the risk of conception exists)

• Glomerular filtration rate (GFR) ≥ 60mL/min

The GFR is to be based on the Cockroft-Gault formula for creatinine clearance

• ASAT ≤ 2.5 x ULN and ALAT ≤ 2.5 x ULN

• Bilirubin ≤ 3 x ULN

• ANC ≥ 1.5 x 109/L

• Platelets ≥ 100 x 109/L

• Hemoglobin ≥ 10 g/dL (without transfusions)

• Sodium and potassium within normal limits or ≤ 10% above or below (supplementation permitted)

All laboratory parameters required to determine subject eligibility will be analyzed at local sites.

Exclusion criteria:

Subjects are not eligible for this study, if they fulfill one or more of the following exclusion criteria:

• Prior chemotherapy. However previous (neo-)adjuvant (radio-)chemotherapy is allowed if it was finished > 1 year prior to start of study treatment and no more than 300 mg/m2 cisplatin has been administered

• Prior treatment with an antibody or molecule targeting EGFR- and/or VEGFR-related signaling pathways

• Brain metastasis and/or leptomeningeal disease (known or suspected)

• Radiotherapy (except localized radiotherapy for pain relief as outlined in section 6.8.2), major surgery or any investigational drug in the 30 days before the start of study treatment

• Concurrent chronic systemic immune or hormone therapy not indicated in this study protocol (except for physiologic replacement)

• Clinically relevant coronary artery disease (NYHA functional angina classification III/IV), congestive heart failure (NYHA III/IV), clinically relevant cardiomyopathy, history of myocardial infarction in the last 12 months, or high risk of uncontrolled arrhythmia

• Active hepatitis B or C

• Chronic diarrhea or short bowel syndrome

• Presence of any contra-indication to treatment with cetuximab, capecitabine and cisplatin including:

• Known hypersensitivity to capecitabine, fluorouracil, cisplatin, cetuximab or to any of the excipients of these drugs

• Known dihydropyrimidine dehydrogenase (DPD) deficiency

• Subjects with hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption

• Current treatment with sorivudine or chemically related analogues, such as brivudine

• Symptomatic peripheral neuropathy NCI-CTCAE grade ≥ 2 and/or ototoxicity NCI-CTC AE grade ≥ 2, except if due to trauma or mechanical impairment due to tumor mass

• Pregnancy or lactation period

• Concurrent treatment with a non-permitted drug (see section 6.8.2)

• Treatment in another clinical study within the past 30 days

• Previous malignancy other than gastric cancer in the last 5 years except for basal cell cancer of the skin or preinvasive cancer of the cervix

• Medical or psychological conditions that would not permit the subject to complete the study or sign informed consent

• Legal incapacity or limited legal capacity

• Significant disease which, in the investigator’s opinion, would exclude the subject from the study

The subjects must fulfill all eligibility criteria to be randomized in this study. No exemptions from any in-/exclusion criteria will be allowed. If any deviation from eligibility is retrospectively detected for an already randomized subject, the investigator and sponsor must decide immediately whether it is safe to treat this subject further within the study